2-(4-Bromobenzyl) tethered 4-amino aryl/alkyl-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-*d*]pyrimidines: Design, Synthesis, anticancer assessment via dual topoisomerase-1/II inhibition, and *in silico* studies

Sahil Arora,[a] Bhagyshree Patra,[b] Isha Dhamija,[b] Santosh Guru,[b] Raj Kumar [a*]

[a]*Laboratory for Drug Design and Synthesis, Department of Pharmaceutical Sciences and Natural Products, School of Pharmaceutical Sciences, Central University of Punjab, Bathinda 151 401 India.*
[b]*Department of Biological Sciences, National Institute of Pharmaceutical Education and Research, Hyderabad, India*

**Corresponding author: Raj Kumar (raj.khunger@cup.edu.in; raj.khunger@gmail.com)*

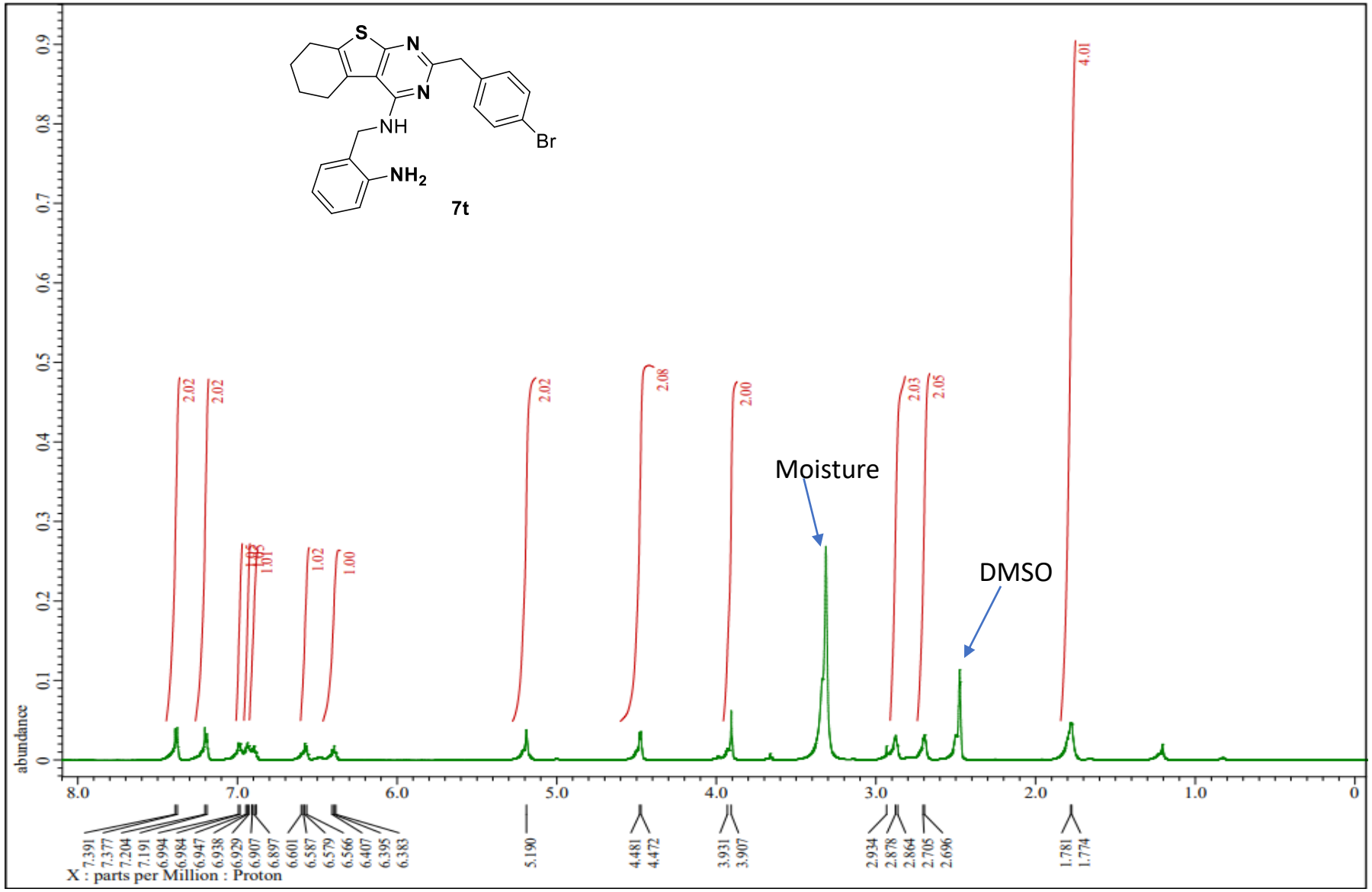

Figure S1 ^{1}H NMR (d_6-DMSO, 600 MHz) of *N*-(2-aminobenzyl)-2-(4-bromobenzyl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-*d*]pyrimidin-4-amine (**7t**)

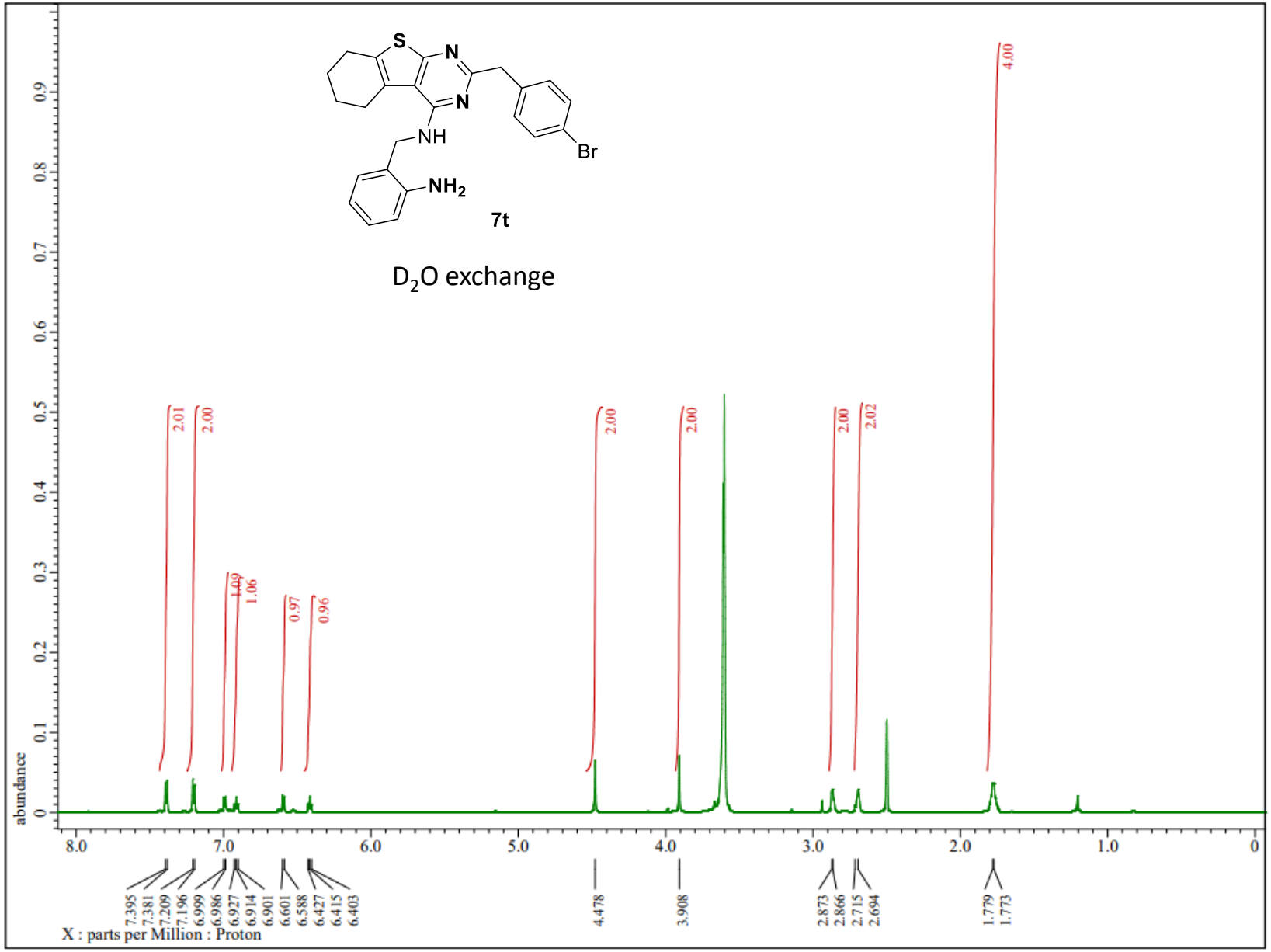

Figure S2 ^{1}H NMR (d_6-DMSO, 600 MHz) of *N*-(2-aminobenzyl)-2-(4-bromobenzyl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-*d*]pyrimidin-4-amine (**7t**)

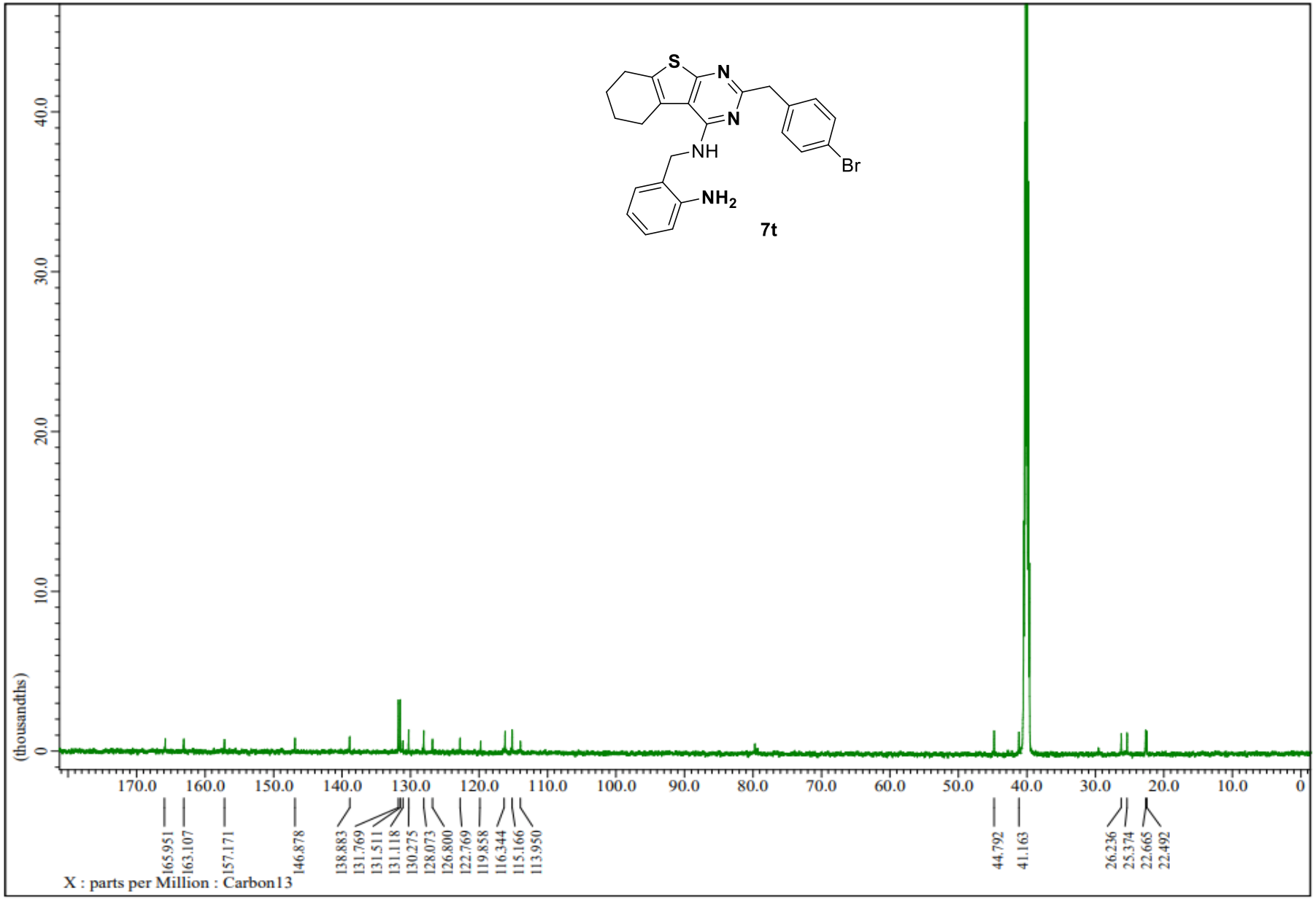

Figure S3 ^{13}C NMR (d_6-DMSO, 151 MHz) of *N*-(2-aminobenzyl)-2-(4-bromobenzyl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-*d*]pyrimidin-4-amine (**7t**)

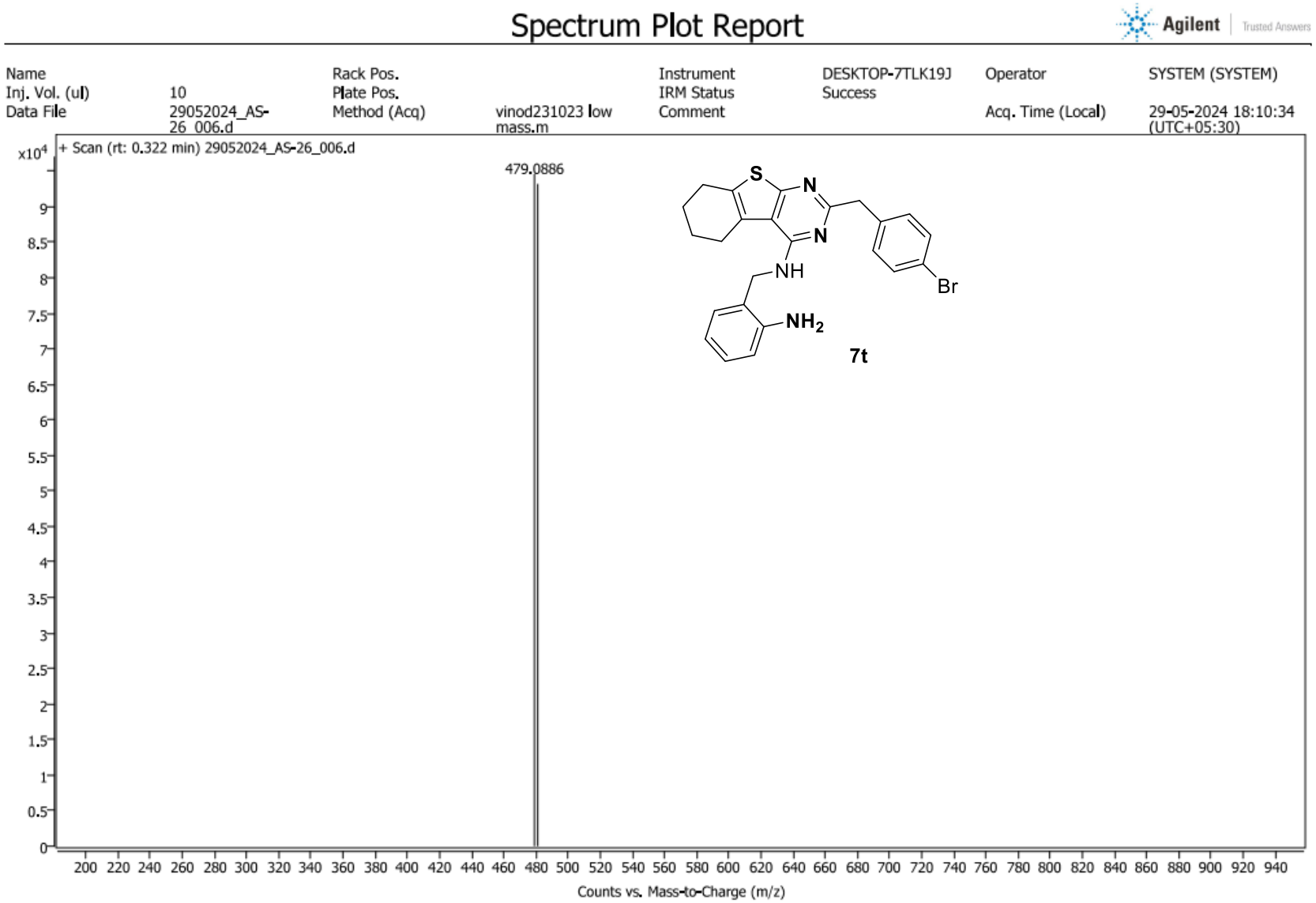

Figure S4 HRMS (ESI-TOF) of *N*-(2-aminobenzyl)-2-(4-bromobenzyl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-*d*]pyrimidin-4-amine (**7t**)

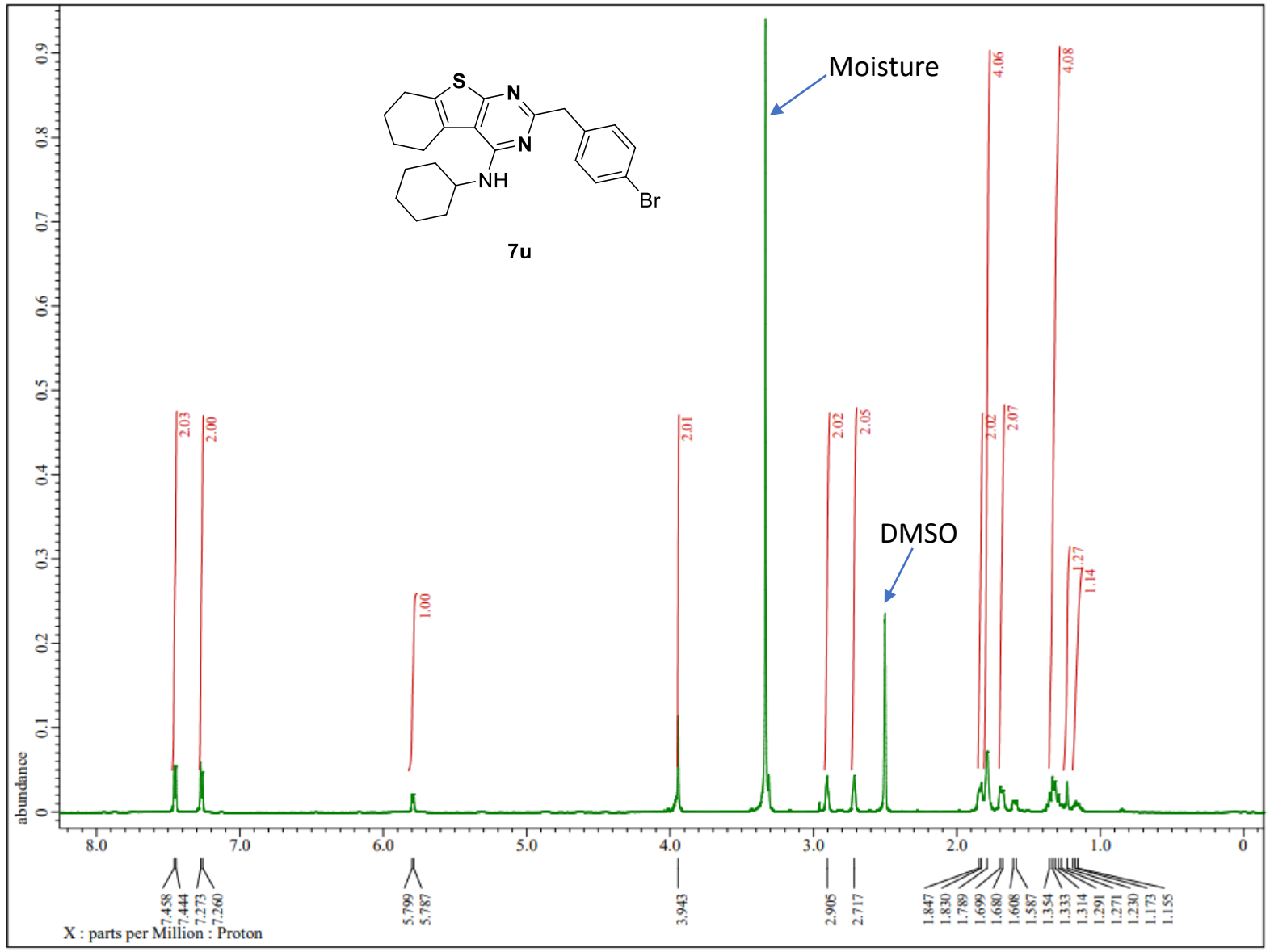

Figure S5 ^{1}H NMR (d_6-DMSO, 600 MHz) of 2-(4-bromobenzyl)-*N*-cyclohexyl-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-*d*]pyrimidin-4-amine (**7u**)

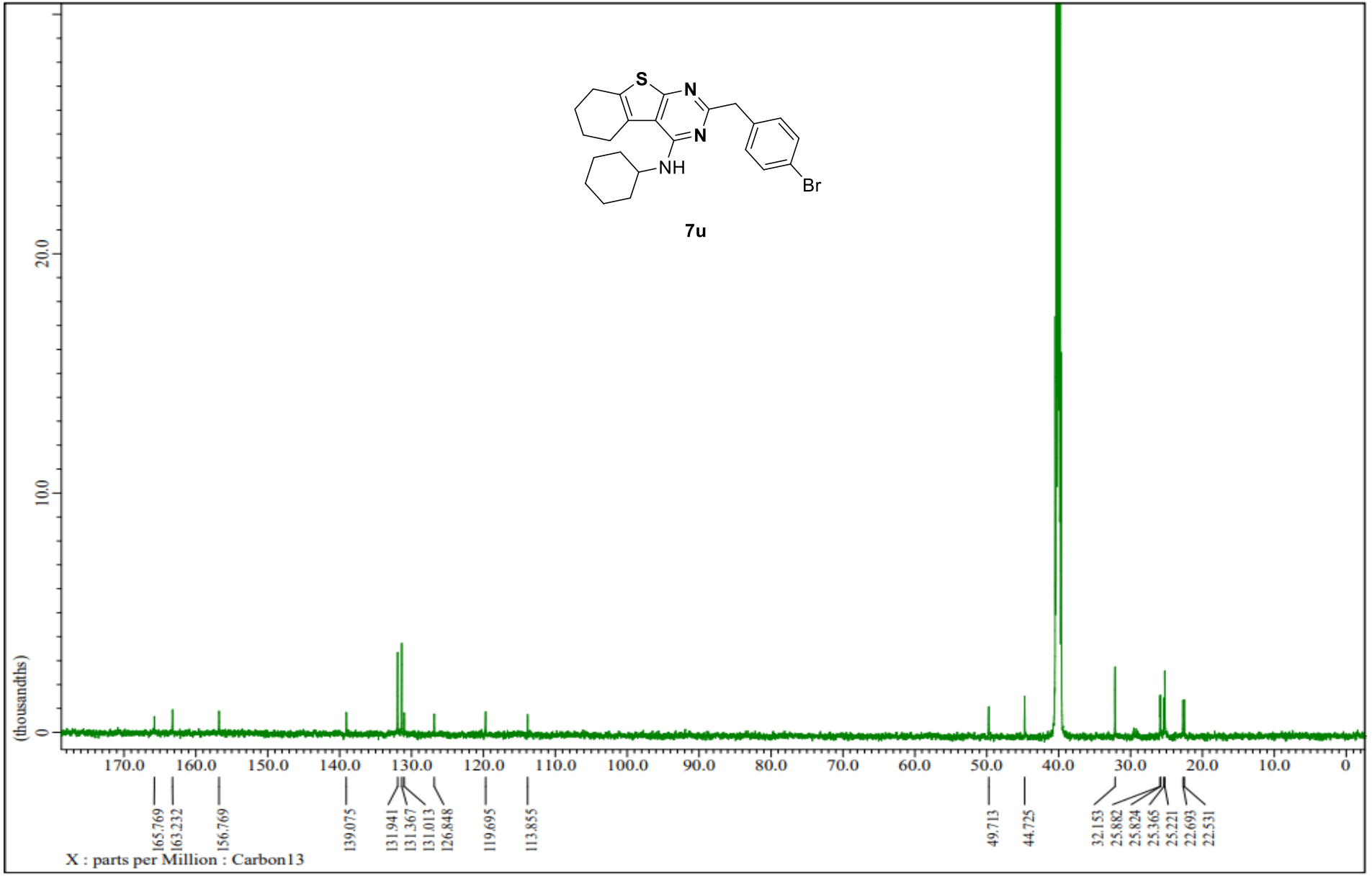

Figure S6 ^{13}C NMR (151 MHz, $CDCl_3$) of 2-(4-bromobenzyl)-*N*-cyclohexyl-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-*d*]pyrimidin-4-amine (**7u**)

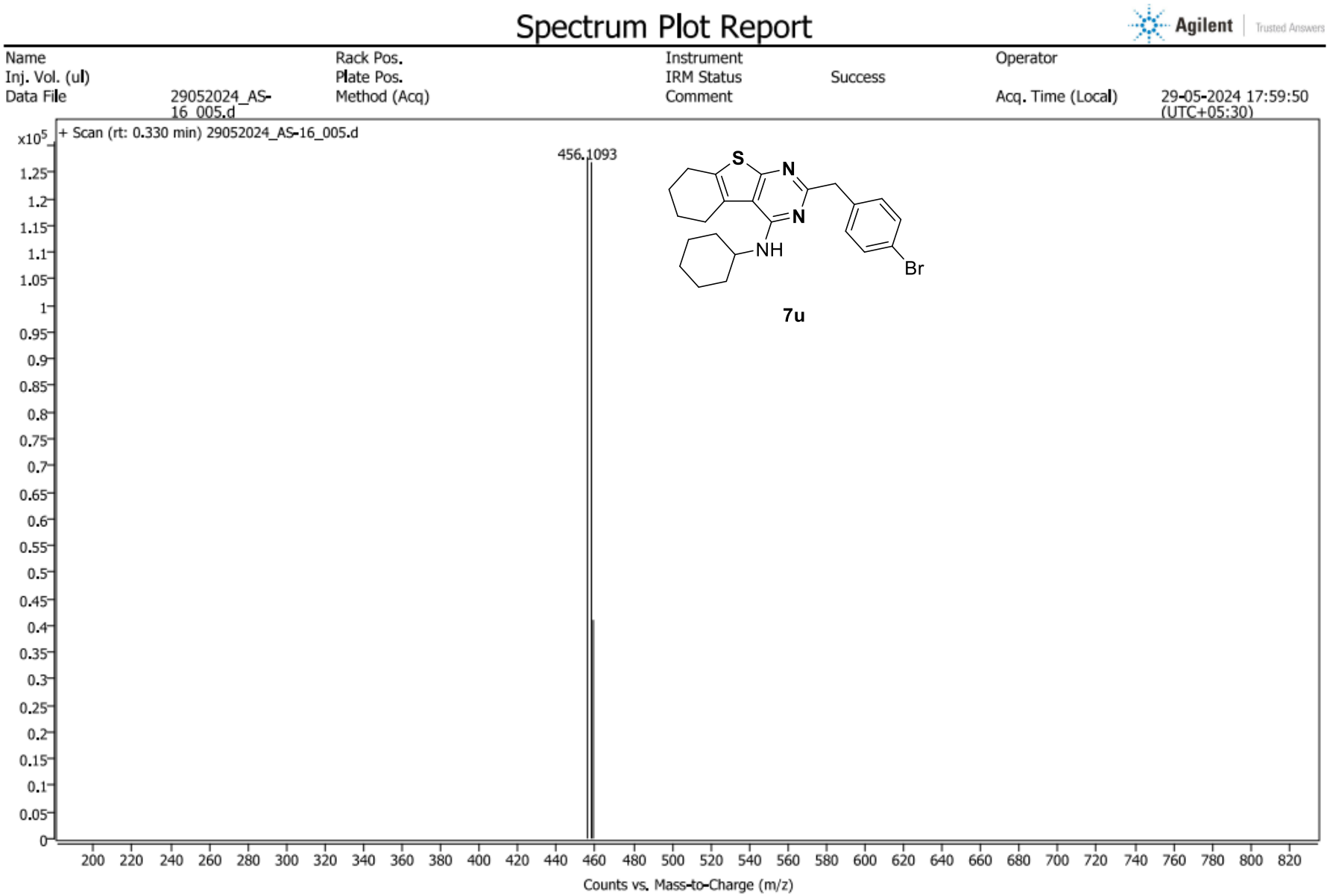

Figure S7 HRMS (ESI-TOF) of 2-(4-bromobenzyl)-*N*-cyclohexyl-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-*d*]pyrimidin-4-amine (**7u**)

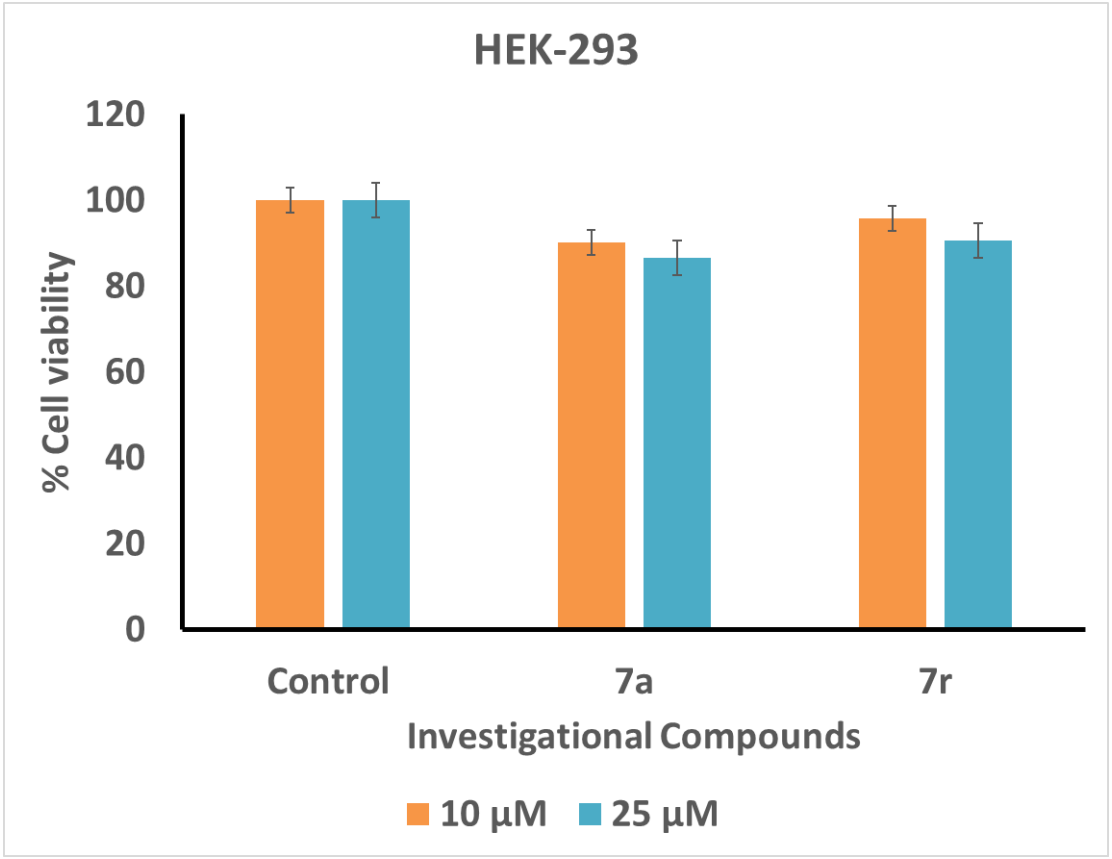

Figure S8 Assessment of cytotoxicity of active compounds 7a and 7r against HEK-293 cells at 10 and 25 µM concentrations.